

Application No. 09/965,703  
Amendment dated April 20, 2005  
Reply to Office Action of November 24, 2004

### REMARKS

The objection to the specification has been withdrawn. The objection to claim 1 has been withdrawn. The rejection of claims 1-3 under 35 U.S.C. § 102(a) has been withdrawn. The rejection of claims 1-6, 11 and 12 under 35 U.S.C. § 103(a) has been withdrawn. Claims 1-7, 11, 12 and 15 are currently under examination in the present application. Claims 1, 3-5 and 11 have been rejected and claims 2, 6, 7, 12 and 15 have been objected to. Claims 1, 7 and 15 have been amended. No new matter has been added. Applicants reserve the right to refile this subject matter in a continuation or divisional application filed during the pendency of this application.

### *Objection*

Claims 7 and 15 were objected to as being drawn to non-elected subject matter. Applicants have amended claims 7 and 15 to recite only the elected subject matter," thereby obviating the basis of the objection.

### *Rejection under 35 U.S.C. § 102(b)*

Claims 1 and 3 were rejected under 35 U.S.C. § 102 (b) as being anticipated by Leonhardt *et al.* (1998). The instant claims are drawn to a gene expression modulation system wherein the first gene expression vector comprises a DBD and a LBD; and a second gene expression vector comprises a transactivation domain and LBD not from USP. The examiner suggests that these claims are anticipated by Leonhardt *et al.* because the reference teaches the use of the mammalian two-hybrid system to examine the role of ligand in the dimerization of human progesterone receptor (hPR). Specifically, the examiner suggests that Leonhardt *et al.* teaches a gene expression system comprising a first construct comprising DBD and a LBD from a nuclear hormone receptor, GAL4 and PR respectively, and a second construct comprising a transactivation domain and a LBD from a nuclear hormone receptor, VP16 and PR, respectively.

Applicants contend that Leonhardt *et al.* teach an assay to determine how agonists and antagonists of the PR affect the dimerization of PR using a two-hybrid system in which the first and second constructs utilize the same ligand binding domain. Leonhardt *et al.* do not teach a gene expression system in which the ligand binding domains of the expression constructs are different.

Application No. 09/965,703  
Amendment dated April 20, 2005  
Reply to Office Action of November 24, 2004

Applicants submit that the present invention is an inducible gene expression system which comprises a first vector comprising a DBD and LBD from a nuclear receptor and a second vector comprising an AD and LBD from a nuclear receptor other than USP, wherein the ligand binding domains from the first polypeptide and the second polypeptide are different.

Leonhardt *et al.* fail to teach or disclose Applicants' invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d, 1913, 1920 (Fed. Cir. 1989). The prior art fails to provide each and every element set forth in the present claims for the reasons set forth above.

Thus, Applicants maintain that the cited prior art fails to teach or disclose the present invention as required to set forth anticipation of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

#### ***Rejection under 35 U.S.C. § 103(a)***

Claims 1, 3-5 and 11 were rejected under 35 U.S.C. § 103(a) as unpatentable over Leonhardt *et al.* in view of Gage *et al.* (U.S. 5,919,667). The examiner states that the instant claims are drawn to a gene expression modulation system wherein the first gene expression vector comprises a DBD and an LBD, wherein the LBD is an ecdysone receptor; and a second gene expression vector which comprises a transactivation domain and LBD not from USP. The examiner submits that the Leonhardt *et al.* reference does not teach a gene expression system wherein the first construct comprises EcR and the second comprises RXR. However, the examiner implies that the '667 patent discloses a transgenic animal that contains one or more expression constructs containing nucleic acid encoding an EcR, exogenous RXR and a heterologous gene under the transcription control of an EcR response element, and therefore it would have been obvious to one of skill in the art to make a gene expression modulation system where the first gene expression vector comprises a DBD and an LBD, wherein the LBD is an ecdysone receptor; and a second gene expression vector which comprises a transactivation domain and LBD not from USP.

Application No. 09/965,703  
Amendment dated April 20, 2005  
Reply to Office Action of November 24, 2004

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons previously presented above, Applicants contend that Leonhardt *et al.* do not teach or suggest all the claim limitations of the present invention, and thus do not support a *prima facie* case of obviousness.

Gage *et al.* teach a MARV vector which can comprise a receptor complex of EcR and RXR, and a MARSHA vector which comprises the gene to be expressed and the response element. Gage *et al.* does not teach the separation of the DBD and AD into the two hybrid format of the present invention. Gage *et al.* does not teach an inducible gene expression system which comprises a first vector comprising a DBD and LBD from a nuclear receptor and a second vector comprising an AD and LBD from a nuclear receptor other than USP. As Leonhardt *et al.* do not teach the use of different LBDs, one of skill in the art would not be motivated to combine these references. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). In the case of Leonhardt *et al.* there is no use or desirability in modifying the LBDs because the purpose of the study is to examine ligand-induced dimerization of the progesterone receptor, and therefore there is no desirability or motivation to combine those teachings with the teachings of Gage *et al.*

The above combination of prior art fails to suggest Applicants' inventions. The prior art fails to provide the required motivation. There is no suggestion or motivation in any of the cited art itself to make these combinations or to further modify these combinations.

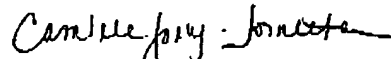
For the reasons set forth above, Applicants maintain that the combination of the cited prior art, when the teachings are taken *as a whole*, fail to supply the motivation required to set forth obviousness of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

BEST AVAILABLE COPY

Application No. 09/965,703  
Amendment dated April 20, 2005  
Reply to Office Action of November 24, 2004

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Therefore, Applicants respectfully request reconsideration and withdrawal of all of the above rejections.

Respectfully submitted,



Camille Jolly-Tornetta, Ph.D.  
Registration No. 48,592

Date: April 20, 2005

RheoGene, Inc.  
2650 Eisenhower Avenue  
Norristown, PA 19403  
Telephone: (610) 650-8734  
Fax: (610) 650-8755

BEST AVAILABLE COPY